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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,482	09/23/2003	Claudio Cavazza	2818-170	9079

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EXAMINER	
KIM, JENNIFER M	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/21/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/667,482	CAVAZZA, CLAUDIO	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/23/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 9-14 are presented for Examination.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 9-14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,653,349B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because it encompasses same subject matter. Instant claims drawn to "preventing" a kidney dysfunction or "providing kidney protection" would obviously

expected from the claims of the patent drawn to the "treatment" or "reducing a kidney dysfunction because the claims in the patent encompasses same method step of administration of same compounds with same effective amounts to the very same subject population.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 9-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "treating a kidney dysfunction", does not reasonably provide enablement for the "preventing a kidney dysfunction". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors**

have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method for preventing a kidney dysfunction or preventing nephropathy caused by a nephrotoxic agent which comprises administering to an individual in need thereof 2-5mg of acetyl L-carnitine and 2-5mg of propionyl L-carnitine/kg body weight/day or an equimolar amount of a pharmacologically acceptable salt thereof. The nature of the invention is extremely complex in that it encompasses the actual prevention of a kidney dysfunction disorder (i.e. nephropathy) such that the subject treated with above compounds does not contract a kidney dysfunction.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass prevention of a complex kidney disorder in humans, which has potentially many different causes (i.e. many different nephrotoxic agents or combination of agents. Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually prevent a kidney dysfunction is minimal. All of the guidance provided by the specification is directed towards treatment rather than prevention of s kidney dysfunction.

Working Examples: All of the working examples provided by the specification are directed toward the treatment rather than prevention of a kidney dysfunction.

State of the Art: While the state of the art is relatively high with regard to treatment of kidney dysfunction (i.e. nephropathy), the state of the art with regard to prevention of such dysfunction is underdeveloped. The state of the art, Suzuki et al. (U.S.Patent No. 5,246,835) report that it is difficult to cure nephropathy of a patient and that nephropathy generally develops into terminal renal insufficiency within 5 or 6 years. (column 1, lines 20-25).

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual prevention of a kidney dysfunction in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of prevention of a kidney dysfunction.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for prevention of kidney dysfunction. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard to prevention of a kidney dysfunction with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage,

duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding prevention of kidney dysfunction with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to prevent the development of kidney dysfunction in a subject by administration of one of the claimed compounds.

Therefore, a method of preventing a kidney dysfunction caused by a nephrotoxic or potential nephrotoxic external agent which comprises administering to an individual in need thereof 2-5mg of acetyl L-carnitine and 2-5mg of propionyl L-carnitine/kg body weight/day or an equimolar amount of a pharmacologically acceptable salt thereof is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 9-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Calvani et al. (U.S. Patent No. 5,955,424).

Calvani et al. teach the pharmaceutical composition comprising L-carnitine or an alkanoyl L-carnitine or a pharmacologically acceptable salts thereof, useful as a medicament for inhibiting nephrotoxicity resulting from the administration of an immunosuppressant drug such as cyclosporine-A, tacrolimus, rapamicine and deoxyspergualine. (abstract). Calvani et al. illustrate tests showing carnitine-induced renal protection with administration of **acetyl L-carnitine** or **propionyl L-carnitine**. (see Experimental tests, column 3-6). Calvani et al. teach the effective amount of L-carnitine in two different doses of 2mg/l and 5mg/l.

Calvani et al. do not expressly teach the composition comprising acetyl L-carnitine and propionyl L-carnitine in a single formulation for inhibiting nephrotoxicity.

It would have been obvious to one of ordinary skill in the art to combine acetyl L-carnitine and propionyl L-carnitine in a single formulation for inhibiting nephrotoxicity because Calvani et al. teach that each of the active agents are effective for the such inhibition. One of ordinary skill in the art would have been motivated to combine acetyl

L-carnitine and propionyl L-carnitine in a single formulation in order to achieve an expected additive benefit of inhibiting nephrotoxicity as illustrated by Calvani et al. One of ordinary skill in the art would have been reasonably expect that the obvious method would provide kidney protection from a kidney dysfunction/nephropathy caused by nephrotoxic agent (cyclosporine, tacrolimus, rapamicine) because each of the active agents has a renal protective effect as demonstrated by Calvani et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Kim
Patent Examiner
Art Unit 1617

Jmk
December 15, 2006